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General Physiology is the study of biological mechanisms through analytical investigations, which decipher the molecular and cellular mechanisms underlying biological function at all levels of organization.

The mission of the *Journal of General Physiology* is to publish articles that elucidate important biological, chemical, or physical mechanisms of broad physiological significance.

EDITORIALS

1 **Editorial practices, scientific impact, and scientific quality.** Olaf Sparre Andersen

3 **Show me the data.** Mike Rossner, Heather Van Epps, and Emma Hill

COMMENTARIES

5 **Mg^{2+}-dependent regulation of BK channels: importance of electrostatics.** Christopher J. Lingle

ARTICLES

13 **Mg^{2+} enhances voltage sensor/gate coupling in BK channels.** Frank T. Horrigan and Zhongming Ma

33 **Disuse-induced preferential loss of the giant protein titin depresses muscle performance via abnormal sarcomeric organization.** Jun Udaka, Shintaro Ohmori, Takako Terui, Iwao Ohtsuki, Shin'ichi Ishiwata, Satoshi Kurihara, and Norio Fukuda

43 **Sulfonylurea receptors type 1 and 2A randomly assemble to form heteromeric K_{ATP} channels of mixed subunit composition.** Kim W. Chan, Adam Wheeler, and László Csanády

59 **KCNE peptides differently affect voltage sensor equilibrium and equilibration rates in KCNQ1 K^+ channels.** Jessica M. Rocheleau and William R. Kobertz

69 **Structural determinants of water permeability through the lipid membrane.** John C. Mathai, Stephanie Tristram-Nagle, John F. Nagle, and Mark L. Zeidel

77 **Theory of passive permeability through lipid bilayers.** John F. Nagle, John C. Mathai, Mark L. Zeidel, and Stephanie Tristram-Nagle

87 **Charge scan reveals an extended region at the intracellular end of the GABA receptor pore that can influence ion selectivity.** Virginia E. Wotring and David S. Weiss

Cover picture: Disuse-induced changes in rat soleus muscles. (Top) Whole muscles taken from the same animal. Bar, 1 cm. (Middle) Electron micrographs. Black arrows, Z-line; yellow arrows, mitochondria; orange arrows, small granule vesicles. Bar, 1 μm. (Bottom) Fluorescence analysis of skinned sarcomeres showing the I-Z-I brush width; black arrows, Z-line; green arrows, thin filament pointed end (see article by Udaka et al., 33–41).

JGP

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MEETING SUMMARY

99 The 61st Symposium of the Society of General Physiologists: ***membrane biophysics of fusion, fission, and rafts in health and disease*** (organized by Frederic Cohen and Joshua Zimmerberg). J. Kevin Foskett

103 Paul F. Cranefield award to Frank T. Horrigan.

COMMENTARIES

105 **To ATP or not to ATP: this is the question.** Alessio Accardi

ARTICLES

109 **The muscle chloride channel ClC-1 is not directly regulated by intracellular ATP.** Giovanni Zifarelli and Michael Pusch

117 **Temperature dependence of fusion kinetics and fusion pores in Ca^{2+}-triggered exocytosis from PC12 cells.** Zhen Zhang and Meyer B. Jackson

125 **Ca^{2+}-activated K^+ channels in murine endothelial cells: block by intracellular calcium and magnesium.** Jonathan Ledoux, Adrian D. Bonev, and Mark T. Nelson

137 **Modular design of Cys-loop ligand-gated ion channels: functional 5-HT_3 and GABA ρ1 receptors lacking the large cytoplasmic M3M4 loop.** Michaela Jansen, Moez Bali, and Myles H. Akabas

147 **Intrinsic electrostatic potential in the BK channel pore: role in determining single channel conductance and block.** Ingrid Carvacho, Wendy Gonzalez, Yolima P. Torres, Sebastian Brauchi, Osvaldo Alvarez, Fernando D. Gonzalez-Nilo, and Ramon Latorre

163 **Agonist-dependent single channel current and gating in $\alpha_4\beta_2\delta$ and $\alpha_1\beta_2\gamma_{2S}$ $GABA_A$ receptors.** Angelo Keramidas and Neil L. Harrison

LETTER TO THE EDITORS

183 **Irreproducible results—a response to Thomson Scientific.** Mike Rossner, Heather Van Epps, and Emma Hill

Cover picture: Electrostatic potential landscape of the BK pore and neutralization mutants. Pseudocolors correspond to the electrostatic potential obtained by solving the Poisson-Boltzmann equation (red, negative; blue, positive). Top figure corresponds to the wild-type BK, middle figure is the neutralization mutant E386N/E389N, and the bottom figure corresponds to the D326N/E329Q (see article by Carvacho et al., 147–161).

JGP

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ARTICLES

185 **Role for SUR2A ED domain in allosteric coupling within the K_{ATP} channel complex.** Amy B. Karger, Sungjo Park, Santiago Reyes, Martin Bienengraeber, Roy B. Dyer, Andre Terzic, and Alexey E. Alekseev

197 **Calmodulin regulation of $Na_V1.4$ current: role of binding to the carboxyl terminus.** Subrata Biswas, Isabelle Deschênes, Deborah DiSilvestre, Yanli Tian, Victoria L. Halperin, and Gordon F. Tomaselli

211 **Inflammatory mediators increase Nav1.9 current and excitability in nociceptors through a coincident detection mechanism.** François Maingret, Bertrand Coste, Françoise Padilla, Nadine Clerc, Marcel Crest, Sergiy M. Korogod, and Patrick Delmas

227 **Ion binding in the open HCN pacemaker channel pore: fast mechanisms to shape "slow" channels.** Alex K. Lyashchenko and Gareth R. Tibbs

245 **Highly Ca^{2+}-selective TRPM channels regulate IP_3-dependent oscillatory Ca^{2+} signaling in the *C. elegans* intestine.** Juan Xing, Xiaohui Yan, Ana Estevez, and Kevin Strange

257 **Gating charge immobilization in Kv4.2 channels: the basis of closed-state inactivation.** Kevin Dougherty, Jose A. De Santiago-Castillo, and Manuel Covarrubias

275 **Troponin and titin coordinately regulate length-dependent activation in skinned porcine ventricular muscle.** Takako Terui, Munguntsetseg Sodnomtseren, Douchi Matsuba, Jun Udaka, Shin'ichi Ishiwata, Iwao Ohtsuki, Satoshi Kurihara, and Norio Fukuda

285 Correction

Cover picture: ED domain in the gating of ATP-sensitive K^+ channels. The ED domain of the SUR2A subunit contributes to the coordination of nucleotide binding domains (NBDs) securing translation of activating (left) and inhibiting (center) signals into the open or closed state of Kir6.2 channels. Disruption of the ED domain stabilizes SUR2A NBDs in a conformation that sustains only residual communication between the channel subunits (right) (see article by Karger et al., 185–196).

JGP

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COMMENTARIES

287 **Connexin specificity of second messenger permeation: real numbers at last.** Andrew L. Harris

ARTICLES

293 **Gap junction channels exhibit connexin-specific permeability to cyclic nucleotides.** Giedrius Kanaporis, Gulistan Mese, Laima Valiuniene, Thomas W. White, Peter R. Brink, and Virginijus Valiunas

307 **Calcium transport mechanisms of PC12 cells.** Joseph G. Duman, Liangyi Chen, and Bertil Hille

325 **Luminal Ca^{2+} regulation of single cardiac ryanodine receptors: insights provided by calsequestrin and its mutants.** Jia Qin, Giorgia Valle, Alma Nani, Alessandra Nori, Nicoletta Rizzi, Silvia G. Priori, Pompeo Volpe, and Michael Fill

335 **Calcium-dependent inactivation terminates calcium release in skeletal muscle of amphibians.** Eduardo Ríos, Jingsong Zhou, Gustavo Brum, Bradley S. Launikonis, and Michael D. Stern

349 **Roles of GRK and PDE4 activities in the regulation of β_2 adrenergic signaling.** Wenkuan Xin, Tuan M. Tran, Wito Richter, Richard B. Clark, and Thomas C. Rich

365 **Tl^+-induced μs gating of current indicates instability of the MaxiK selectivity filter as caused by ion/pore interaction.** Indra Schroeder and Ulf-Peter Hansen

379 **Chloride homeostasis in *Saccharomyces cerevisiae*: high affinity influx, V-ATPase-dependent sequestration, and identification of a candidate Cl^- sensor.** Michael L. Jennings and Jian Cui

Cover picture: (Top) Phase and fluorescence micrographs of a cell pair in which intercellular cAMP diffusion was examined. For detection and identification purposes, reporter cells were transfected with SpIH channels (green fluorescence) and nontransfected donor cells labeled with RFP (red fluorescence). (Bottom) Current traces showing the increase in the SpIH current as a result of cAMP diffusion from the donor cell via gap junctions (see article by Kanaporis et al., 293–305).

JGP

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EDITORIALS

393 **Introducing Edward N. Pugh, Jr.** Olaf Sparre Andersen

PERSPECTIVES

395 **Perspectives on how to drug an ion channel.** Olaf Sparre Andersen

399 **Ion channels as drug targets: the next GPCRs.** Gregory J. Kaczorowski, Owen B. McManus, Birgit T. Priest, and Maria L. Garcia

407 **Antibody-based validation of CNS ion channel drug targets.** Kenneth J. Rhodes and James S. Trimmer

415 **How to validate a heteromeric ion channel drug target: assessing proper expression of concatenated subunits.** Jon T. Sack, Oleg Shamotienko, and J. Oliver Dolly

421 **Lipid bilayer–mediated regulation of ion channel function by amphiphilic drugs.** Jens A. Lundbæk

431 **How highly charged anionic lipids bind and regulate ion channels.** Stephen J. Tucker and Thomas Baukrowitz

COMMENTARIES

439 **Zebrafish—topical, transparent, and tractable for ultrastructural studies.** John M. Squire, Carlo Knupp, and Pradeep K. Luther

ARTICLES

445 **Structure and function of skeletal muscle in zebrafish early larvae.** Ying Dou, Monika Andersson-Lendahl, and Anders Arner

455 **A role for DPPX modulating external TEA sensitivity of Kv4 channels.** Olaia Colinas, Francisco D. Pérez-Carretero, José R. López-López, and M. Teresa Pérez-García

473 **Clearance of extracellular K^+ during muscle contraction—roles of membrane transport and diffusion.** Torben Clausen

483 **An extracellular Cu^{2+} binding site in the voltage sensor of BK and shaker potassium channels.** Zhongming Ma, Kin Yu Wong, and Frank T. Horrigan

503 **Cholesterol promotes hemifusion and pore widening in membrane fusion induced by influenza hemagglutinin.** Subrata Biswas, Shu-Rong Yin, Paul S. Blank, and Joshua Zimmerberg

Cover picture: Site and mechanism of Cu^{2+} action in BK channels. Putative Cu^{2+}-coordinating residues (labeled) from BK channel mSlo1 are mapped onto the voltage sensor structure of a Kv1.2/Kv2.1 chimera (Long et al., 2007), viewed from side (left) and top (right). A gating scheme (center) proposes that Cu^{2+} binding stabilizes the resting voltage sensor (R) (see article by Ma et al., 483–502).

JGP

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EDITORIALS

515 **Models and mechanistic insight.** Edward N. Pugh Jr. and Olaf S. Andersen

521 **You wrote it; you own it!** Emma Hill and Mike Rossner

BRIEF REVIEWS

523 **Voltage-gated Na channel selectivity: the role of the conserved domain III lysine residue.** Gregory M. Lipkind and Harry A. Fozzard

COMMENTARIES

531 **S0, where is it?** Diane M. Papazian

ARTICLES

537 **Position and role of the BK channel α subunit S0 helix inferred from disulfide crosslinking.** Guoxia Liu, Sergey I. Zakharov, Lin Yang, Shi-Xian Deng, Donald W. Landry, Arthur Karlin, and Steven O. Marx

549 **Atomic constraints between the voltage sensor and the pore domain in a voltage-gated K^+ channel of known structure.** Anthony Lewis, Vishwanath Jogini, Lydia Blachowicz, Muriel Lainé, and Benoît Roux

563 **A continuum method for determining membrane protein insertion energies and the problem of charged residues.** Seungho Choe, Karen A. Hecht, and Michael Grabe

575 **NGF inhibits M/KCNQ currents and selectively alters neuronal excitability in subsets of sympathetic neurons depending on their M/KCNQ current background.** Zhanfeng Jia, Junjie Bei, Lise Rodat-Despoix, Boyi Liu, Qingzhong Jia, Patrick Delmas, and Hailin Zhang

589 **KCNQ1 and KCNE1 in the I_{Ks} channel complex make state-dependent contacts in their extracellular domains.** Xulin Xu, Min Jiang, Kai-Ling Hsu, Mei Zhang, and Gea-Ny Tseng

605 **MEC-2 and MEC-6 in the *Caenorhabditis elegans* sensory mechanotransduction complex: auxiliary subunits that enable channel activity.** Austin L. Brown, Zhiwen Liao, and Miriam B. Goodman

617 **Surface expression of epithelial Na channel protein in rat kidney.** Gustavo Frindt, Zuhal Ergonul, and Lawrence G. Palmer

Cover picture: (Top) The crystal structure of the Kv1.2 channel (gray) and a structural model of the open activated conformation (color) deduced from electrophysiological data and molecular dynamics simulations. The pore domain is green, the S2 is yellow, S3 is red, and S4 is blue. The open conformation is stabilized by a His-Zn^{2+}-His metal bridge between R294 in S4 and position A351 in S5. (Bottom) The electrophysiological data used to constrain the modeling. (Left) The open-activated state of the Kv1.2 channel is stabilized by the formation of the His-Zn^{2+}-His metal bridge, as reflected in the left shift of the G(V) curve. (Right) The bridge has high affinity with a half-maximal Zn^{2+} concentration ~360 nM.